

Claims:

1. A method for determining the mechanical strength of an atherosclerotic plaque comprising subjecting an excised plaque to force or pressure means and measuring the
5 amount of force or pressure required to rupture the plaque.
2. An *ex vivo* method for determining the force or pressure required to rupture an atherosclerotic plaque, comprising excising the part of the vessel housing the plaque from an animal, applying a force or pressure to the plaque and measuring the amount of force or
10 pressure required to cause plaque rupture.
3. A method for determining the ability of a test compound to enhance plaque stability comprising administering a test compound to an animal possessing an atherosclerotic plaque, excising the plaque, subjecting the excised plaque to pressure or force means, measuring the
15 amount of pressure or force required to rupture the plaque and based on this value relative to a control value assessing whether or not the compound enhances plaque stability.
4. A method for determining the ability of a test compound to enhance plaque stability comprising:
20 (i) administering a test compound to a non-human animal possessing atherosclerotic plaques;
(ii) excising a plaque containing vessel segment from the animal;
(iii) exerting physical force to the plaque from step (ii);
(iv) measuring the amount of physical force required to rupture the plaque;
25 (v) carrying out steps (i) to (iv) but with a control animal that has not been treated with the test compound;
(vi) comparing the amount of plaque rupture force from step (iv) and (v) and, if the plaque rupture force from step (iv) is greater than that from step (v) identifying the test compound as one that enhances plaque stability.
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5. The method according to claim 4, wherein the test animal has been induced to develop atherosclerotic plaques by dietary feeding.

6. The method according to claim 4, wherein the test animal is a transgenic or knock-out animal.
7. The method according to claim 6, wherein the knock-out animal is a single or double
5 knock-out animal.
8. The method according to claim 6 or 7, wherein the animal has a defunct LDL receptor.
9. The method according to claim, 6 or 7, wherein the animal has a defunct APO E
10 receptor.
10. The method according to any of claims 6 to 9, wherein the animal is a mouse.
11. The method according to claim 4, wherein the test animal is of an age where the
15 plaque size has stabilised.
12. The method according to claim 4, wherein the test animal is of an age where the
plaque size is still growing/increasing.
- 20 13. A method according to any of claims 2, 3 or 4, wherein the animal is selected from the
group consisting of: mouse, rat, gerbil, hamster, guinea pig, rabbit, dog, cat, monkey, pig,
sheep, cow and goat.
14. The method according to claim 4, wherein the physical force applied to the plaque in
25 step (iii) is tensile force.
15. The method according to claim 4, wherein the physical force applied to the plaque in
step (iii) is carried out by mounting the plaque in a holder and allowing a solid member to
push against the inside of the vessel opposed to the plaque and measuring the amount of force
30 required to cause plaque rupture.
16. The method according to any of the preceding claims, wherein the amount of force is
measured using a force transducer.

17. The method according to claim 16, wherein plaque rupture is determined by change in first derivative.
18. The method according to any of the preceding claims, wherein plaque rupture is
5 determined visually.
19. The method according to any of the preceding claims, wherein plaque rupture is observed using a microscope.
- 10 20. The method according to any of the preceding claims, wherein plaque rupture is observed using a camera.
21. The method according to claim 4, wherein the physical force applied to the plaque in step (iii) is positive or negative pressure effected by pushing or sucking a liquid against the
15 plaque-burdened vessel.
22. The method according to any of the preceding claims, wherein more than one plaque from each animal is tested.
- 20 23. A method as claimed in any of the preceding claims, wherein the plaque is an aortic plaque.
24. Use of an excised plaque in an assay to measure plaque mechanical strength.
- 25 25. A method for determining whether or not a compound has potential in treating or preventing cerebro- or cardiovascular events due to plaque rupture, comprising testing the ability of the compound to enhance plaque stability in an ex vivo plaque stability assay.
26. A method for determining whether or not a compound has potential in treating or
30 preventing cerebro- or cardiovascular events due to plaque rupture, comprising testing the ability of the compound to enhance plaque stability according to the method of claim 1.

27. The method according to claim 25 or 26, wherein the cardiovascular event is primary or secondary myocardial infarction.

28. A device for determining the mechanical strength of a plaque comprising means for
5 securing a plaque-burdened vessel and means for exerting a physical force on the plaque
burdened vessel.

29. The device according to claim 28, which also comprises means for measuring the
physical force.

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30. A device for measuring of the rupture strength of a material, in particular, a biological
material by means of measuring the force required to rupture said material said device
comprising means to retain said material, means to provide a rupture force tending to rupture
said retained material and means to measure said force when said material ruptures.

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31. A device for measuring of the rupture strength of a material, in particular, a biological
material as claimed in claim 30 wherein said material comprises an atherosclerotic plaque.

32. A device for measuring of the rupture strength of a material, in particular, a biological
20 material as claimed in claim 30 or 31 wherein said means to retain said material comprises a
pair of adjacent members.

33. A device for measuring of the rupture strength of a material, in particular, a biological
material as claimed in any one of claims 30 to 32 wherein said adjacent members comprise
25 discs.

34. A device for measuring of the rupture strength of a material, in particular, a biological
material as claimed in any one of claims 30 to 33 wherein said means to provide a rupture
force comprises a rigid member.

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35. A device for measuring of the rupture strength of a material, in particular, a biological
material as claimed in any one of claims 30 to 34 wherein said rigid member comprises a rod.

36. A device for measuring of the rupture strength of a material, in particular, a biological material as claimed in any one of claims 30 to 35 wherein said rod is driven forward by means of a micro motor.
- 5 37. A device for measuring of the rupture strength of a material, in particular, a biological material as claimed in any one of claims 30 to 35 wherein said means to provide a rupture force comprises a stream of fluid.
38. A device for measuring of the rupture strength of a material, in particular, a biological
10 material as claimed in any one of claims 30 to 36 wherein said means to measure said force when material ruptures comprises a force displacement transducer.
39. A method of measuring the rupture strength of a material, in particular, a biological material comprising the steps of providing said material, retaining said material, providing a
15 force tending to rupture said material and measuring said force required to rupture said material.
40. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in claim 39 wherein said material comprises an atherosclerotic plaque.
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41. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in claim 39 or 40 wherein said retaining of said material is by means of a pair of adjacent members.
- 25 42. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in any one of claims 39 to 41 wherein said adjacent members comprise discs.
43. A method of measuring the rupture strength of a material, in particular, a biological
30 material as claimed in any one of claims 39 to 42 wherein said force tending to rupture said material is provided by means of a rigid member

44. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in any one of claims 39 to 43 wherein said rigid member comprises a rod.

45. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in any one of claims 39 to 44 wherein said rod is driven forward by means of a micro motor.

46. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in any one of claims 39 to 44 wherein said means to provide a rupture force comprises a stream of fluid.

47. A method of measuring the rupture strength of a material, in particular, a biological material as claimed in any one of claims 39 to 46 wherein said means to measure said force when material ruptures comprises a force displacement transducer.